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Dated: January 10, 2005

Signature:

*Mary Jane DiPalma*  
(Mary Jane DiPalma)

Docket No.: CWRU-P03-015  
(PATENT)

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Patent Application of:  
Gerson et al.

Application No.: 10/505400

Confirmation No.: 7253

Filed: August 19, 2004

Art Unit: N/A

For: ALKYLATING AGENT COMBINATIONS  
IN THE TREATMENT OF CANCER

Examiner: Not Yet Assigned

**INFORMATION DISCLOSURE STATEMENT (IDS)**

MS Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

Pursuant to 37 CFR 1.56, 1.97 and 1.98, the attention of the Patent and Trademark Office is hereby directed to the references listed on the attached PTO/SB/08. It is respectfully requested that the information be expressly considered during the prosecution of this application, and that the references be made of record therein and appear among the "References Cited" on any patent to issue therefrom.

This Information Disclosure Statement is filed before the mailing date of a first Office Action on the merits as far as is known to the undersigned (37 CFR 1.97(b)(3)).

Copies of the references on the PTO/SB/08 are not provided because copies of published U.S. patent documents are not required for this application and/or they were previously cited by or submitted to the Office in prior application numbers 10/079049, filed February 19, 2002, and 09/373,693 filed August 13, 1999

In accordance with 37 CFR 1.97(g), the filing of this Information Disclosure Statement shall not be construed to mean that a search has been made or that no other material information as defined in 37 CFR 1.56(a) exists. In accordance with 37 CFR 1.97(h), the filing of this

Information Disclosure statement shall not be construed to be an admission that any patent, publication or other information referred to therein is "prior art" for this invention unless specifically designated as such.

It is submitted that the Information Disclosure Statement is in compliance with 37 CFR 1.98 and the Examiner is respectfully requested to consider the listed references.

The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 18-1945, under Order No. CWRU-P03-015. A duplicate copy of this paper is enclosed.

Dated: January 10, 2005

Respectfully submitted,

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PTO/SB/08A (10-01)

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<b>Substitute for form 1449A/PTO</b>  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)				<b>Complete if Known</b>	
				Application Number	10/505,400
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				First Named Inventor	Stanton L. Gerson
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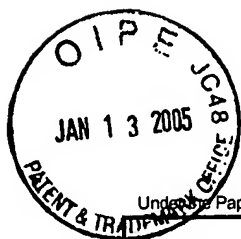
U.S. PATENT DOCUMENTS					
Examiner Initials*	Cite No. <sup>1</sup>	Document Number Number-Kind Code <sup>2</sup> (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	AA	5,731,304	03-1998	Baer et al.	
*	AB	6,465,448	10/15/02	Gerson et al.	

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
		Country Code <sup>3</sup> -Number <sup>4</sup> -Kind Code <sup>5</sup> (if known)				
	AC	JP 10045589	02/1998			
	AD	WO 94/15615	07/1994			

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<sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> See attached Kinds Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.04. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the application number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS					
Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, page(s), volume-issue number(s), publisher, city and/or country where published.			T <sup>2</sup>
	AE	Ahnen. Colon Cancer Prevention by NSAIDs: What is the Mechanism of Action? Eur. J. Surg. 582, 111-114 (1998).			
	AF	Bianchi et al. O6-methylguanine-DNA Methyltransferase Activity and Induction of Novel Immunogenicity in Murine Tumor Cells Treated with Methyhlating Agents. Cancer Chemother. Pharmacol. 29, 277-282 (1992).			
	AG	Boulton et al. Potentiation of temozolomide-induced cytotoxicity: a comparative study of the biological effects of poly (ADP-ribose) polymerase inhibitors. Br. J. Cancer 72, 849-856 (1995).			
	AH	Branch et al. Defective mismatch binding ad a mutator phenotype in cells tolerant to DNA damage. Nature 362, 652-654 (1993).			
	AI	Buschfort et al. DNA excision repair profiles of normal and leukemic human lymphocytes: functional analysis at the single-cell level. Cancer Res. 57, 651-658 (1997).			
	AJ	Caldecott et al. XRCC1 polypeptide interacts with DNA polymerase-beta and possibly poly (ADP-ribose) polymerase, and DNA ligase III is a novel molecular 'nick-sensor' in vitro. Nucleic Acids Res. 24, 4387-4394 (1996).			
		Chou and Talalay. "Quantitative analysis of dose-effect relationship: the combined effects of			
Examiner Signature				Date Considered	



PTO/SB/08A (10-01)

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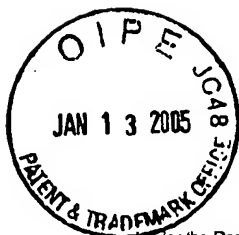
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Sheet	2	of	5	Attorney Docket Number	CWRU-P03-015

AK	multiple drugs on enzyme inhibitors," in Advances in Enzyme Regulation, G. Weber, ed. New York: Pergamon Press, p. 27-55 (1983).	
AL	Choy et al. Concurrent Paclitaxel, Carboplatin, and Radiation Therapy for Locally Advanced Non-small Cell Lung Cancer. Seminars in Oncology 26, Suppl. 2: 36-43 (1999).	
AM	Claij et al. Microsatellite Instability in Human Cancer: A Prognostic Marker for Chemotherapy? Exper. Cell Res. 246, 1-10 (1999).	
AN	Coquerelle et al. Overexpression of N-methylpurine-DNA glycosylase in Chinese hamster ovary cells renders them more sensitive to the production of chromosomal aberrations by methylating agents: a case of imbalanced DNA repair. Mutation Res. 336, 9-17 (1995).	
AO	De Murcia, J.M. et al. Requirement of poly (ADP-ribose) polymerase in recovery from DNA damage in mice and in cells. PNAS 94, 7303-7304 (1997).	
AP	Engelward et al. Repair-deficient 3-methyladenine DNA glycosylase homozygous mutant mouse cells have increased sensitivity to alkylation-induced chromosome damage and cell killing. EMBO J. 15, 945-952 (1996).	
AQ	Fink et al. The role of DNA mismatch repair in drug resistance. Clin. Cancer Res. 4, 1-6 (1998).	
AR	Gonzaga et al. Identification of the cross-link between human O6-methylguanine-DNA methyltransferase and chloroethylnitrosourea-treated DNA. Cancer Res. 52, 6052-6058 (1992).	
AS	Griffin et al. DNA mismatch binding and incision at modified guanine bases by extracts of mammalian cells: implications for tolerance to DNA methylation damage. Biochemistry 33, 4787-4793 (1994).	
AT	Gunderson. Indications for and Results of Combined Modality Treatment of Colorectal Cancer. Acta Oncologica 38, 7-21 (1999).	
AU	Hainsworth et al. The Current Role and Future Prospects of Paclitaxel in the Treatment of Small Cell Lung Cancer. Seminars in Oncology 26, Suppl. 2: 60-66 (1999).	
AV	Kaina et al. Chromosomal instability, reproductive cell death and apoptosis induced by O6-methylguanine in Mex-, Mex+ and methylation-tolerant mismatch repair compromised cells: facts and models. Mutation Res. 381, 227-241 (1997).	
AW	Karran and Bignami. DNA damage tolerance, mismatch repair and genome instability. BioEssays 16, 833-839 (1994).	
AX	Kat et al. An alkylation-tolerant, mutator human cell line is deficient in strand-specific mismatch repair. PNAS 90, 6424-6428 (1993).	
AY	Kerr et al. Novel therapeutic strategies for colorectal cancer. Hosp. Med. 59, 617-621 (1998).	

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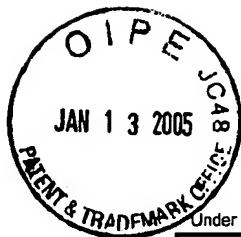
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AZ	Kingma and Osheroff. Apurinic sties are position-specific topoisomerase II poisons. J. Biol. Chem. 272, 1148-1155 (1997).
BA	Lazebnik et al. Cleavage of poly(ADP-ribose) polymerase by a proteinase with properties like ICE. Nature 371, 346-347 (1994).
BB	Lindahl et al. Post-translation modification of poly(AD-P-ribose) polymerase induced DNA strand breaks. Trends Biochem. Scil 20, 405-411 (1995).
BC	Link et al. Basic research supported developments of chemotherapy in nonresectable isolated colorectal liver metastases to a protocol of hepatic artery infusion using mitoxantrone, 5-FU + folinic acid and mitomycin C. Gan To Kagaku Ryoho 26, 269-281 (1999).
BD	Liu et al. Mismatch repair mutations override alkyltransferase in conferring resistance to temozolomide by not to 1,3-bis(2-chloroethyl)nitrosourea. Cancer Res. 56, 5375-5379 (1996).
BE	Liu, L. et al. Clin. Cancer Res. 5, 2908-2917 (1999).
BF	Liu, L. et al. Methoxyamine Mediated Inhibition of Base Excision Repair (BER) Significantly Enhances Temozolomide Antitumor Effect in Mismatch Repair (MMR) Proficient and Deficient Colon Cancer Xenografts. Proc. Am. Assoc. Cancer Res. 41, 98 (March 2000).
BG	Malapetsa et al. Identification of a 116 kDa protein able to bind 1,3-bis (2-chloroethyl)-1-nitrosourea-damaged DNA as poly (ADP-ribose) polymerase. Mutation Res. 362, 41-50 (1996).
BH	Matijasevic et al. Protection against chloroethylnitrosourea cytotoxicity by eukaryotic 3-methyladenine DNA glycosylase. PNAS 90, 11855-11859 (1993).
BI	Midgley et al. Colorectal Cancer. Lancet 353, 391-399 (1999).
BJ	Mitchell and Dolan. Effect of temozolomide and dacarbazine on O6-alkylguanine-DNA alkyltransferase activity and sensitivity of human tumor cells and xenografts to 1,3-bis(2-chloroethyl)-1-nitrosourea. Cancer Chemother. Pharmacol. 32, 59-63 (1993).
BK	Molinete et al. Over production of the poly (ADP-ribose) polymerase beta. Mutation Res. 407, 203-215 (1998).
BL	Morris et al. Flow cytometric evaluation of cell-cycle progression in ethyl methanesulfonate and methyl methanesulfonate-exposed P3 cells: relationship to the induction of sister-chromatid exchanges and cellular toxicity. Environ. Mol. Mutagen. 18, 139-149 (1991).
BM	Neddermann et al. Cloning and Expression of Human G/T Mismatch-specific Thymine-DNA Glycosylase. J. Biol. Chem. 271, 12767-12774 (1996).
BN	Neijt et al. Paclitaxel/Carboplatin for the Initial Treatment of Advanced Ovarian Cancer. Seminars in Oncology 26, Suppl. 2: 78-83 (1999).

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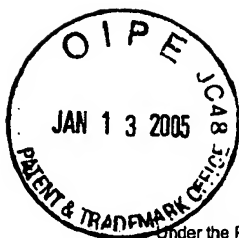
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	BO	O'Connor et al. Isolation and structure of a cDNA expressing a mammalian 3-methyladenine-DNA glycosylase. EMBO J. 9, 3337-3342 (1990).	
	BP	Olsen et al. Molecular cloning of human uracil-DNA glycosylase, a highly conserved DNA repair enzyme. EMBO J. 8, 3121-3125 (1989).	
	BQ	Pegg et al. Structure, function and inhibition of O6-alkylguanine-DNAAGT. Prog. Nucleic Acid Res. Mol. Biol. 51, 167-233 (1995).	
	BR	Pera et al. Exceptional sensitivity of testicular germ cell tumour cell lines to the new anti-cancer agent, tomozolomide. Br. J. Cancer 71, 904-906 (1995).	
	BS	Perez. Paclitaxel Plus Nonanthracycline Combinations in Metastatic Breast Cancer. Seminars in Oncology 26, Suppl. 2, 21-26 (1999).	
	BT	Prakash and Gibson. Sequence-selective depurination, DNA interstrand cross-linking and DNA strand break formation associated with alkylated DNA. Carcinogenesis 13, 425-431 (1992).	
	BU	Radicella et al. Cloning and characterization of hOOG1, a human homolog of the OGG1 gene of Saccharomyces cerevisiae. PNAS 94, 8010-8015 (1997).	
	BV	Robertson et al. Down-regulation of apurinic/aprimidinic endonuclease expression is associated with the induction of apoptosis in differentiating myeloid leukemia cells. Cell Growth and Differentiation 8, 443-449 (1997).	
	BW	Rosenquist et al. Cloning and characterization of a mammalian 8-oxoguanine DNA glycosylase. PNAS 94, 7429-7434 (1997).	
	BX	Samson et al. Cloning and characterization of a 3-methyladenine DNA glycosylase cDNA from human cells whose gene maps to chromosome 16. PNAS 88, 9127-9131 (1991).	
	BY	Sobol et al. Requirement of mammalian DNA polymerase-beta in base-excision repair. Nature 379, 183-186 (1996).	
	BZ	Taverna, P. et al. Methoxyamine (MX) Potentiates DNA Single Strand and Double Strand Breaks Induced by Temozolomide (TMZ) in Colon Cancer Cells. Proc. Am. Assoc. Cancer Res. 41, 265 (March 2000).	
	CA	Tentori et al. Role of Wild-Type p53 on the Antineoplastic Activity of Temozolomide Alone or Combined with Inhibitors of Poly(ADP-Ribose) Polymerase. J. Pharmacol. Exp. Ther. 285, 884-893 (1998).	
	CB	Tentori, L. et al. Cytotoxic and clastogenic effects of a DNA minor groove binding methyl sulfonate ester in mismatch repair deficient leukemia cells. Leukemia 14, 1451-1459 (2000).	
	CC	Thomale et al. Haematol. Blood Transfus. 39, 3-12 (1998).	

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	CD	Vollberg et al. Isolation and characterization of the human uracil DNA glycosylase gene. PNAS 86, 8693-8697 (1989).	
	CE	Von Hoff. Promising New Agents for Treatment of Patients with Colorectal Cancer. Seminars in Oncology 25, Suppl 11: 47-52 (1998).	
	CF	Walker et al. A role for the human DNA repair enzyme HAP1 in cellular protection against DNA damaging agents and hypoxic stress. Nucleic Acids Res. 22, 4884-4889 (1994).	
	CG	Wedge et al. 3-Aminobenzamide and/or O6-benzylguanine evaluated as an adjuvant to temozolomide or BCNU treatment in cell lines of variable mismatch repair status and O6-alkylguanine-DNA alkyltransferase activity. Br. J. Cancer 74, 1030-1036 (1996).	
	CH	Wedge et al. In vitro evaluation of temozolomide combined with X-irradiation. Anti-Cancer Drugs 8, 92-97 (1997).	
	CI	Wedge et al. Effect of single and multiple administration of an O6-benzylguanine/temozolomide combination: an evaluation in a human melanoma xenograft model. Cancer Chemother. Pharmacol. 40, 266-272 (1997).	
	CJ	Wilson et al. Life without DNA repair. PNAS 94, 12754-12757 (1997).	
	CK	Wilson. Mammalian base excision repair and DNA polymerase beta. Mutation Res. 407, 203-215 (1998).	

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